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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/700,906	11/04/2003	Benjamin Oshlack	200.1133CON5	1129

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EXAMINER	
SHEIKH, HUMERA N	

ART UNIT	PAPER NUMBER
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/700,906	OSHLACK ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *75-78* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *75-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/17/07; 7/13/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Response and Amendment after Non-Final Office Action and Applicant's Arguments/Remarks, all filed 04/30/07 and the Information Disclosure Statements (IDS) filed 05/17/07 and 07/13/07 is acknowledged.

The 35 U.S.C. non-statutory obviousness-type double patenting rejections of claims 62-74 over claims of 10/689,866, 10/700,861 and 10/700, 893 have been withdrawn, by virtue of Applicant's persuasive remarks.

The following are the new grounds of rejection:

Claims 75-78 are pending in this action. Claims 1-61 were previously cancelled. Claims 62-74 have been cancelled herein. New claims 75-78 have been added. Claims 75-78 are rejected.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 75-78 are rejected under 35 U.S.C. 102(b) as being anticipated by Kreek et al. (U.S. Pat. No. 4,987,136).

Kreek et al. ('136) disclose oral sustained release dosage forms that comprise effective amounts of an opioid antagonist, such as naloxone, naltrexone, nalmefine and related compounds (col. 1, lines 59-66); (col. 2, lines 4-62).

Polymeric carriers are disclosed that include carnauba wax, cellulose esters and ethers, fats, keratin, gluten or various natural or synthetic esters (col. 5, lines 63-68). The polymeric carrier is comprised in amounts of from about 80% to 95% (col. 6, lines 58-65).

* * * * *

Claims 75, 76 and 78 are rejected under 35 U.S.C. 102(b) as being anticipated by Palermo (WO 99/32120).

Palermo (WO '120) discloses an oral dosage form of an opioid analgesic, comprising an analgesically effective amount of an opioid agonist together with an opioid antagonist, the amount of opioid antagonist including being sufficient to counteract opioid effects if extracted together with the opioid agonist (see p. 6, lines 1-18). Suitable opioid antagonists disclosed include naltrexone, naloxone, nalmephene, cyclazocine and levallorphan. A most preferred antagonist is naltrexone (p. 11, lines 14-19); (p. 13, lines 14-31).

In preferred embodiments, the substrate (e.g., tablet core bead, matrix particle) containing the opioid analgesic is coated with a hydrophobic material selected from (i) an alkylcellulose; (ii) an acrylic polymer or (iii) mixtures thereof (p. 22, lines 6-14).

* * * * *

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 75-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Palermo (WO 99/32120).

Palermo (WO '120) teaches an oral dosage form of an opioid analgesic, comprising an analgesically effective amount of an opioid agonist together with an opioid antagonist, the amount of opioid antagonist including being sufficient to counteract opioid effects if extracted together with the opioid agonist (see p. 6, lines 1-18).

In certain preferred embodiments, the opioid agonist is hydrocodone, hydromorphone, oxycodone, morphine or pharmaceutically acceptable salts thereof (p. 7, lines 5-6). Suitable

opioid antagonists disclosed include naltrexone, naloxone, nalmephene, cyclazocine and levallorphan. A most preferred antagonist is naltrexone (p. 11, lines 14-19); (p. 13, lines 14-31). In certain preferred embodiments of the method, the opioid agonist and the opioid antagonist are combined in a ratio of opioid antagonist to opioid agonist which is analgesically effective when the combination is administered orally, but which is aversive in a physically dependent subject (p. 7, lines 7-15). In embodiments where the opioid is hydrocodone and the antagonist is naltrexone, the ratio of naltrexone to hydrocodone is preferably from about 0.03-0.27:1 by weight (p. 7, lines 15-26).

Palermo teaches that the dosage forms of the invention may be liquids, tablets, multiparticulates, dispersible powders or granules, hard or soft capsules, lozenges, aqueous or oily suspensions, emulsions, syrups, elixirs, microparticles , buccal tablets, etc. (p. 7, lines 27-31); (p. 8, line 29 – p. 9, line 1). In certain preferred embodiments, the oral dosage forms are sustained release formulations. This may be accomplished via the incorporation of a sustained release carrier into a matrix containing the opioid agonist and opioid antagonist; or via a sustained release coating of a matrix containing the opioid agonist and opioid antagonist, where the sustained release coating contains at least a portion of the sustained release carrier included in the dosage form (p. 8, lines 1-9); (p. 20, lines 16-21).

With regards to ratios, Palermo teaches that the combinations of opioid antagonists/opioid agonists which are orally administered in ratios which are equivalent to the ratio of e.g., naltrexone to hydrocodone set forth are considered to be within the scope of the invention. For example, in some embodiments, naloxone is utilized as the opioid antagonist, the amount of naloxone included in the dosage form being large enough to provide an

equiantagonistic effect as if naltrexone were included in the combination (p. 19-31). This demonstrates bioequivalency of the dosage forms.

Palermo teaches that the dosage forms may be coated with one or more materials suitable for the regulation of release or the protection of the formulation. The coatings are provided to permit either pH-dependent or pH-independent release (p.21, lines 18-29).

In preferred embodiments, the substrate (e.g., tablet core bead, matrix particle) containing the opioid analgesic is coated with a hydrophobic material selected from (i) an alkylcellulose; (ii) an acrylic polymer or (iii) mixtures thereof (p. 22, lines 6-14).

Suitable and preferred alkylcellulose polymers taught include ethylcellulose (p. 22, lines 19-25). Acrylic polymers are also disclosed and include acrylic acid and methacrylic acid copolymers, methyl methacrylate copolymers, ethoxyethyl methacrylates, cyanoethyl methacrylate, poly(acrylic acid), poly(methacrylic acid) and the like (p. 23, line 10 – p. 24, line 22); (p. 29, lines 7-18). Plasticizers can also be included in the composition (p. 24, line 24 – p. 25, line 20). A process for preparing coated beads is disclosed at p. 25, line 21 – p. 28, line 8. Matrix bead formulations are disclosed at page 28. Hydrophilic and/or hydrophobic materials, such as gums, cellulose ethers, acrylic resins, protein derived materials and any pharmaceutically acceptable hydrophobic material or hydrophilic material, which is capable of imparting, controlled release of the active agent and which melts (or softens to the extent necessary to be extruded) may be used in this invention (p. 28, lines 19-30).

With regards to amounts of hydrophobic material claimed, the Examiner notes that suitable or effective amounts can be determined by one of ordinary skill in the art through routine or manipulative experimentation to obtain optimal results as these are variable

parameters attainable within the art. Moreover, generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

The Palermo reference explicitly recognizes and teaches oral dosage forms comprising opioid agonists in combination with opioid antagonists, whereby the dosage forms are effective for the substantial reduction of pain. Given the teachings of Palermo discussed above, the instant invention, when taken as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

* * * * *

Claims 75-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over O'Malley et al. (U.S. Pat. No. 6,004,970) in view of Whitmire (U.S. Pat. No. 6,120,806) OR Palermo (WO 99/32120).

O'Malley ('970) teaches an opioid antagonist composition in oral administration forms such as tablets and capsules (col. 3, lines 58-67). The opioid antagonists taught include nalmefene, naloxone, naltrexone or a mixture of any of these (col. 3, lines 1-3).

O'Malley does not teach a hydrophobic material.

Whitmire ('806) teaches an oral controlled release dosage form comprising an opioid antagonist (see Abstract). The oral dosage form comprises the opioid antagonist and

hydrophobic material in a matrix form. Suitable materials are disclosed at column 10, line 37 – col. 11, line 8).

* * * * *

The teachings of O'Malley are discussed above. O'Malley does not teach a hydrophobic material.

Palermo ('120) teaches an oral dosage form of an opioid analgesic, comprising an analgesically effective amount of an opioid agonist together with an opioid antagonist, the amount of opioid antagonist including being sufficient to counteract opioid effects if extracted together with the opioid agonist (see p. 6, lines 1-18). Suitable opioid antagonists disclosed include naltrexone, naloxone, nalmephene, cyclazocine and levallorphan. A most preferred antagonist is naltrexone (p. 11, lines 14-19); (p. 13, lines 14-31). In preferred embodiments, the substrate (e.g., tablet core bead, matrix particle) containing the opioid analgesic is coated with a hydrophobic material selected from (i) an alkylcellulose; (ii) an acrylic polymer or (iii) mixtures thereof (p. 22, lines 6-14).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the hydrophobic materials as taught by either Whitmire or Palermo within the formulations of O'Malley. One of ordinary skill in the art would be motivated to do so with a reasonable expectation of success because both Whitmire and Palermo recognize and teach the inclusion of routinely used hydrophobic materials in their inventions, effective for their sustained release properties. The expected result would be an improved controlled release pharmaceutical dosage form for the treatment of pain.

Response to Arguments

Applicant's arguments, see response on pages 3-5, filed 04/30/07, with respect to the rejection(s) of claim(s) 62-74 under the non-statutory obviousness-type double patenting rejection over claims of the '861, '866 and '893 applications have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of the Kreek et al. ('136) and Palermo ('120) references. Palermo, as discussed above, teaches oral dosage forms comprising opioid agonists and opioid antagonists. The dosage forms can be contained in tablets, multiparticulates, capsules and can be formulated in sustained and controlled release dosage forms.

Conclusion

--No claims are allowed at this time.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday, Tuesday, Thursday and Friday during regular business hours. (Wednesdays - Telework).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Humera N. Sheikh

Primary Examiner

Art Unit 1615

July 23, 2007

HUMERA N SHEIKH
PRIMARY EXAMINER

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